

Critical Liver Support

ADVANCED Naturals PRODUCT MONOGRAPH

Product composition

Medicinal Ingredients:

Each capsule contains:

Milk Thistle Seed (<i>Silybum marianum</i>) - 70%/140 mg Silymarin	200 mg
Alpha Lipoic Acid	200 mg
N-Acetyl-Cysteine	100 mg
Garlic bulb (<i>Allium sativum</i>) – 3500 ppm/0.44 mg allicin	125 mg
Vitamin C (Ascorbic acid)	50 mg
Artichoke leaf (<i>Cynara scolymus</i>) 4:1 extract (equivalent to 100 mg)	25 mg
Dandelion root (<i>Taraxacum officinale</i>) 4:1 extract (equivalent to 100 mg)	25 mg
Turmeric rhizome (<i>Curcuma longa</i>) 4:1 extract (equivalent to 100 mg)	25 mg
Selenium (selenomethionine)	100 mcg

Non-medicinal ingredients: Hypromellose

Recommended dose: Adults: Take 3 capsules per day.

Duration of use: Use for a minimum of 3 weeks to see beneficial effects.

Indication:

- Hepatoprotectant/liver protectant.
- Used in Herbal Medicine to help support liver function.
- An antioxidant for the maintenance of good health.

Contraindications: Do not use if you are pregnant, breastfeeding, if you have a bile duct obstruction and/or if you have liver or gall bladder disorders, and/or bowel obstruction.

Discontinue use if you develop symptoms of liver trouble. Consult a health care practitioner if symptoms persist or worsen.

Warnings: Keep out of reach of children.

Consult a health care practitioner prior to use if you have diabetes, gallstones, stomach ulcers or excess stomach acid, have a history of non-melanoma skin cancer, are taking blood thinners, antiplatelet medication or protease inhibitors.

Precautions: Not to be used by children

Adverse Effects: Hypersensitivity, such as allergy, has been known to occur; in which case, discontinue use.

Overdose: For management of suspected product overdose it is recommended to contact your physician.

Symptoms of Overdose: Has not been investigated nor any reports have been filed

Supporting Research and Traditional Evidence

Milk Thistle Seed (*Silybum marianum*) - 70%/140 mg Silymarin

Milk thistle (*Silybum marianum*) has been used traditionally as a hepatoprotectant/liver protectant supportive of liver function, and to offer relieve from digestive disturbances/dyspepsia. (NHPD monograph). Preparations are usually standardized to a concentration of 70 to 80% of three flavonolignans (silibinin, silychristin and silydianin), collectively known as silymarin. Safety is well established in preparations equivalent to 3-14.5 g dried fruit/seed per day; preparations equivalent to 140-600 mg silymarin (calculated as silibinin/silybin) per day. (Mills and Bone, 2000; Blumenthal et al, 2000).

Chronic alcoholic liver damage is partly due to the lipoperoxidation of hepatic cell membranes and anti-oxidizing agents may be useful in treating or preventing damage due to free radicals. Milk thistle extract acts to stabilize hepatic cell membranes, providing hepatocellular protection. Clinical studies suggest or confirm its efficacy in various hepatic disorders including hepatitis A and alcoholic cirrhosis. (Bradley, 2006; Hoffmann, 2003; Blumenthal et al, 2000; Mills and Bone, 2000)

In an 8-week randomized, double-blind, placebo-controlled study to examine the effect of silymarin in acute hepatitis, 105 patients with acute clinical hepatitis and elevated serum alanine aminotransferase (ALT) levels (greater than 2.5 times the upper limit of normal) received either 140 mg silymarin or a vitamin (placebo) 3 times daily (tid) for 4 weeks. Patients were followed-up for 4 weeks. Signs of acute hepatitis and results of liver function tests were recorded on Day 2, 4 and 7, and at Week 2, 4, and 8. Patients treated with silymarin showed quicker resolution of symptoms related to biliary retention (i.e., dark urine, jaundice, and scleral icterus) compared to placebo. Indirect bilirubin

was also significantly decreased in patients treated with silymarin 140 mg tid for 4 weeks. Direct bilirubin, ALT and aspartate aminotransferase (AST) were not significantly reduced. No adverse events were reported; silymarin was well tolerated at the doses administered. (El-Kamary et al, 2009)

In a 12-month open-label, controlled study to examine the effects of silymarin in lipoperoxidation and insulin resistance in diabetes with cirrhosis, 60 patients with insulin-treated diabetes and alcoholic cirrhosis received either 600 mg silymarin per day plus standard therapy or standard therapy alone (control group). Fasting blood glucose levels, glucosuria levels, glycosylated hemoglobin (HbA1c) and malondialdehyde levels were measured. Significant decreases in fasting blood glucose, mean daily blood glucose levels, daily glucosuria and HbA1c levels were observed following 4 months of treatment. Significant decreases in fasting insulin levels and mean insulin requirements were also observed in the treated group; controls showed significant increases in fasting insulin levels and a stabilized insulin need. Findings were consistent with significant decreases in basal and glucagon-stimulated C-peptide levels in the treated group; significant increases in both parameters were reported in the control group. Researchers suggested that silymarin may reduce lipoperoxidation in cell membranes and may reduce insulin resistance. (Velussi et al, 1997)

Alpha Lipoic Acid

Alpha lipoic acid (ALA) provides a source of antioxidants in the maintenance of good health. (NHPD monograph). Its antioxidant effects are similar in mechanism of action to glutathione (GSH), an important endogenous antioxidant; and acts to increase levels of (reduced) GSH. Clinical trials have shown improvement in neuropathic deficits with ALA treatment. In diabetic neuropathy, mechanisms of peripheral nerve dysfunction may be attributed to microvascular damage and hypoxia due to nitric oxide inactivation by free radical activity. ALA may delay or reverse peripheral diabetic neuropathy through its multiple antioxidant properties. (Vallianou et al, 2009). Patients in end-stage renal disease and receiving hemodialysis often experience inflammation, among other morbidities, often the result of increased oxidative stress. Providing antioxidant therapies consisting of ALA, cholecalciferol, ascorbic acid, and gamma-tocopherol may reduce overall inflammation and improve outcomes in these patients. (Sharma et al, 2010).

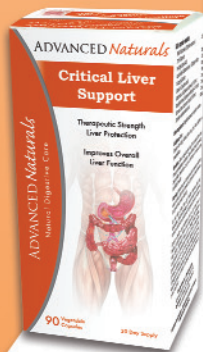
The effects of alpha-lipoic acid (600 mg per day for more than 3 months) on markers of oxidative stress were examined in a cross-sectional study of 107 patients with diabetes mellitus. Plasma lipid hydroperoxides (ROOHs), and ratio of oxidative stress to antioxidant defence (ROOH/(alpha-tocopherol/cholesterol) were measured. Significantly lower ROOHs and a low ratio of ROOH/(alpha-tocopherol/cholesterol), irrespective of glycemic control and micro- or macroalbuminuria were observed. Treatment with alpha-lipoic acid significantly improved imbalances between oxidative stress and antioxidant defence in patients with poor glycemic control and albuminuria. (Borcea et al, 1999)

In a 4-month prospective study to assess the effect of lipoic acid alone and in combination with alpha-tocopherol (AT) on measures of oxidative stress, 31 healthy subjects received either lipoic acid 600 mg/day or AT 400 IU/day for 2 months, and in combination for 2 months more. Urine F2-isoprostanes, plasma protein carbonyl, and low-density lipoprotein (LDL) oxidative susceptibility was measured at baseline, and at 2 and 4 months. Results showed that supplementation with lipoic acid antioxidant decreases plasma- and LDL-oxidation and urinary isoprostanes. (Marangon et al, 1999).

N-Acetyl-Cysteine

N-acetyl cysteine (NAC) is included in the formulation as another source of antioxidants in the maintenance of good health. NAC, a cysteine pro-drug, acts to increase GSH levels and is known for its ability to counter acetaminophen toxicity. It is a safe and well-tolerated antidote for cysteine and GSH deficiency, the latter often associated with numerous pathological conditions. NAC has been used successfully to treat GSH deficiency in a wide range of infections, genetic defects and metabolic disorders, including HIV infection and COPD. Studies suggest a role for NAC as a liver protectant.

In a randomized, double-blind placebo-controlled study to examine the effects of NAC on liver blood flow during early septic shock,



60 patients received either NAC (150 mg/kg bolus dose intravenously over 15 minutes followed by 12.5 mg/kg/hr as continuous infusion) or placebo within 24 hours of the onset of septic shock. In septic shock, decreased splanchnic blood flow is observed despite adequate systemic hemodynamics; plasma appearance of monoethylglycineylidide (MEGX) was used to assess microsomal liver function. Following treatment with NAC, hepatosplanchnic flow and function improved, suggesting enhanced nutritive blood flow. The increase of liver blood flow index was not caused by redistribution to the hepatosplanchnic area, but by an increase of cardiac index. Because of its correlation with liver blood flow index, MEGX may be helpful in identifying patients who benefit from NAC treatment in early septic shock. The results of the study suggested that treatment with NAC may have beneficial effects on liver function. (Rank *et al*, 2000)

In a placebo-controlled pilot study to evaluate the effects of NAC in ischemia-reperfusion injury following liver transplantation, 60 patients received either NAC or placebo (5% glucose solution). Improvements in portal vein and arterial blood flow, reduction in postoperative liver damage and decreases in damage associated with reperfusion were observed. NAC was considered to be a promising substance for reducing graft dysfunction in clinical liver transplantation. (Thies *et al*, 1998).

Garlic bulb (*Allium sativum*) – 3500 ppm/0.44 mg allicin

Garlic bulb has been used traditionally to help relieve symptoms associated with upper respiratory tract infections and catarrhal conditions, to reduce elevated blood lipid levels/ hyperlipidaemia and to help maintain cardiovascular health (NHPD Monograph). Garlic is included in the formulation as a source of antioxidants in the maintenance of good health (ESCOF 2003), and in support of healthy blood lipid levels, indirectly supporting liver function and health.

In a 12-week double-blind, randomized, placebo-controlled intervention study to evaluate the effects of garlic supplementation in hypercholesterolemia, 48 patients with hypercholesterolemia received dietary counselling (recommendations for low-fat intake) and received either 9.6 mg allicin (as garlic powder tablets) or matching placebo. Significant reductions in total cholesterol and LDL-cholesterol were observed in the treated group vs. placebo. No significant difference in triglycerides or in LDL/HDL ratio was observed between groups. Results suggested that garlic supplementation has cholesterol-lowering effects, mediated in part by its direct action and through the effects of nutrient intake. (Kannar *et al*, 2001)

Vitamin C (Ascorbic acid)

Vitamin C is included in the formulation as an antioxidant for the maintenance of good health, and more generally, as a factor in the maintenance of good health. (NHPD Monograph)

Artichoke leaf (*Cynara scolymus*) 4:1 extract (equivalent to 100 mg)

Artichoke leaf has been used traditionally for its diuretic, choleric, hypocholesterolaemic, hypolipidaemic, and hepatostimulating properties. (Newall *et al*, 1996; Bradley, 2006) Artichoke leaf is included in the formulation as a minor supportive ingredient.

Dandelion root (*Taraxacum officinale*) 4:1 extract (equivalent to 100 mg)

Dandelion root has been used traditionally for disturbances of bile flow, stimulation of diuresis, loss of appetite, and dyspepsia. (NHPD Monograph; Blumenthal *et al*, 2000) The NHPD recognizes dandelion root as effective with an established safety profile when taken in recommended doses. It is included in this formulation as a minor supportive ingredient aimed at assisting liver function.

Turmeric rhizome (*Curcuma longa*) 4:1 extract (equivalent to 100 mg)

Turmeric rhizome has been used traditionally to help relieve flatulent dyspepsia (carminative), aid digestion (NHPD Monograph), and for its cholecystokinetic and anti-inflammatory action (Blumenthal *et al*, 2000) The pharmacological constituent in turmeric root responsible for its choleric properties is curcumin, which acts on the gallbladder to increase bile secretion. The herb has a good safety profile when taken at recommended doses of 1.5 – 3 g of daily (Blumenthal *et al*, 2000). The ingredient is a minor supportive ingredient to the primary ingredient and listed claims.

Selenium (selenomethionine)

Selenium has been used traditionally as an antioxidant for the maintenance of good health and more generally, as a factor in maintaining good health. (NHPD Monograph) The ingredient is a minor supportive ingredient to the primary ingredient and listed claims.

Ingredient Summary

Milk Thistle Seed (*Silybum marianum*) – 70%/140 mg Silymarin

- Hepatoprotectant/liver protectant.
- Used in Herbal Medicine to help support liver function.

Alpha Lipoic Acid

- An antioxidant for the maintenance of good health.

N-Acetyl-Cysteine

- An antioxidant for the maintenance of good health.

Garlic bulb (*Allium sativum*) – 3500 ppm/0.44 mg allicin

- An antioxidant for the maintenance of good health.
- To help reduce elevated blood lipid levels/ hyperlipidaemia in adults.

Vitamin C (Ascorbic acid)

- An antioxidant for the maintenance of good health

Artichoke leaf (*Cynara scolymus*) 4:1 extract (equivalent to 100 mg)

- Used traditionally for its hepatostimulating properties.

Dandelion root (*Taraxacum officinale*) 4:1 extract (equivalent to 100 mg)

- Used traditionally for disturbances of bile flow.

Turmeric rhizome (*Curcuma longa*) 4:1 extract (equivalent to 100 mg)

- Used traditionally to increase bile secretion.

Selenium (selenomethionine)

- An antioxidant for the maintenance of good health.

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